REMARKS

I. Allowable subject matter

Applicants thank the Examiner for acknowledging that claims 89 and 91-96 are directed to allowable subject matter.

II. Preliminary remarks

Claims 89, 91-96, 101-106 and 110 are pending. Claims 97-100 and 107-109 are withdrawn for being drawn to a non-elected invention.

Claims 94-95 have been amended to be consistent with the affinity language of claim 101. Claims 101-106 are amended herein to recite "conjugate or fusion protein" as suggested by the Examiner. Claim 102 is amended herein to recite an "isolated" polypeptide. Support for this amendment can be found, for example, at pages 4, 11 and 15 of the application as filed. Claim 110 is added herein to mirror the Examiner's suggested claim language at page 4 of the action. Accordingly, no new matter has been added.

The amendments made herein were made solely to expedite prosecution and not for reasons pertaining to patentability. Applicants reserve the right to pursue the subject matter of any claim (whether original, amended or canceled) in continuing applications.

III. The rejection of claims 101-106 under 35 U.S.C. § 112, first paragraph (enablement), should be withdrawn.

In the action, the Examiner maintained the rejection of claims 101-106 as allegedly failing to be supported by an enabling disclosure. The Examiner does not appear to dispute enablement of antibodies or antigen binding fragments thereof directed to the protein encoded by SEQ ID NO: 1, nor does the Examiner dispute enablement of conjugating or fusing antibodies or antibody fragments to peptide moieties and non-peptide moieties. See page 4 and page 5, lines 5-11 of the action.

The rejection appears to be two-fold. First, the Examiner asserts that the "specification fails to provide guidance how to make a polypeptide (a chain of amino acids joined by peptide bonds) comprising an antibody, or antibody fragment thereof (which is a dimer or tetramer of polypeptide)." Applicants respectfully dispute the Examiner's assertion

that a polypeptide must be a single linear chain of amino acids. The specification does not define the term "polypeptide" in this manner, nor is the Examiner's assertion an art-accepted definition. For example, the abstract attached as Exhibit A characterizes *heterodimeric* insulin composed of A and B chains as a "polypeptide." Desiderio et al., Biomed Mass Spectrom. 1984 Feb;11(2):55-9, Exhibit A ("Fast atom bombardment mass spectral data are presented for the *polypeptides* insulin, oxidized insulin A-chain, carboxymethylated insulin B-chain, and glucagon [emphasis added].")

The rejection should be withdrawn because the action does not point to any evidence supporting the Examiner's interpretation of the term "polypeptide," while Applicants have provided evidence that the term "polypeptide" encompasses multi-chain polypeptides. Nevertheless, solely to expedite prosecution, Applicants have amended the claims to recite "conjugate" or "fusion protein" in accordance with the Examiner's suggestions. The Examiner acknowledges enablement of antibodies or antibody fragments fused to peptide moieties. See page 5, lines 5-11 of the action.

Applicants also respectfully dispute the Examiner's characterization of an antibody or antibody fragment as a dimer or tetramer. Prior to the earliest filing date of the present application, it was routine in the art to screen for single chain antibodies, using a phage display technique in which a single chain composed of fused heavy and light chain variable domains was displayed on the surface of bacteriophage. See Bird et al., Science, 242:423-426, 1988 (Exhibit B). A variety of embodiments of single chain antibodies were well known in the art and described in the specification. For example, the application states:

> . . . the chains may be covalently coupled either directly for example via a disulfide bond between the two variable domains, or through a linker, for example a peptide linker, to form a single chain domain (abbreviated hereinafter as scFv). (Page 34, lines 2-14 of the application as filed)
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> . . . portions or fragments, such as Fab and Fv fragments, of antibodies may also be constructed utilizing conventional enzymatic digestion or recombinant DNA techniques to incorporate the variable regions of a gene which encodes a specifically binding antibody. . . . . large amounts of a single-chain protein containing a fusion of the V_H and V_L domains may be produced (see Bird et al., Science 242:423-426, 1988).

(Page 47, line 20 through page 48, line 5 of the application as filed.)

Thus, contrary to the Examiner's assertions, it was routine in the art to produce a single chain polypeptide antibody or antibody fragment that binds to a specified protein. Second, the Examiner asserts that the specification does not provide sufficient guidance for the "broad genus" of "antibody or antigen binding fragment thereof linked to any protein/peptide." However, the specification discloses how to make and use antibodies that bind to the protein encoded by SEQ ID NO: 1 and also teaches how to make and use fusion and conjugate proteins (see, for example pages 5, 6 and 49 of the application as filed).

Moreover, the art is replete with examples of a polypeptide comprising an antibody (or antibody fragment), wherein the antibody in the fusion protein binds its antigen with the same specificity as the antibody alone. For example, Challita-Eid et al. (J. Immunol., 160:3419-3426, 1998; set forth in Exhibit C) reports the construction and characterization of a fusion protein comprising the T cell costimulatory ligand B7.1 fused to an anti-HER2/neu IgG3 antibody. Another example of a fusion protein comprising an antibody is reported in Gidolf et al. (Blood, 89:2089-2097, 1997; set forth in Exhibit D). Gidolf et al. discloses a fusion protein comprising the Fab fragment of an anti-CD19 antibody and a staphylococcal enterotoxin A (SEA) D227A mutant, wherein the Fab fragment in the fusion protein retains its ability to bind to CD19. Hu et al. (Cancer Res., 56:4998-5004, 1996; set forth in Exhibit E) discloses a fusion protein comprising a chimeric Lym-1 antibody linked to IL-2. Siemers et al. (Bioconjug. Chem., 8:510-519, 1997; set forth in Exhibit F) reports the construction and characterization of a fusion protein comprising a L49-ScFv antibody fragment fused to β-lactamase. Thus, it is clear from the foregoing that it was routine state-of-the-art knowledge prior to the earliest filing date of the present application to construct a polypeptide comprising an antibody (or antibody fragment). The Examiner has not provided any evidence describing the difficulty of generating such polypeptides. Accordingly, because of the guidance in the application as filed, the well known nature of antibodies, and the high level of skill and predictability in the art prior to the filing date of the present application, one of skill in the art would be able to make and use the polypeptide recited in claims 101-106 without undue experimentation. See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In view of the foregoing, Applicants request that the rejection of claims 101-106 as allegedly failing to be supported by an enabling disclosure be withdrawn.

IV. The obviousness-type double-patenting rejection is moot.

The Examiner rejected claims 89 and 91-96 under the judicially created doctrine of obviousness-type double-patenting over claims 1-8 of U.S. Patent No. 6,803,453 because Applicants previously filed a terminal disclaimer containing an inadvertent typographical error. The rejection is moot in view of the terminal disclaimer correctly identifying U.S. Patent No. 6,803,453 submitted with the U.S. Patent and Trademark Office on January 11, 2010. Accordingly, the obviousness-type double patenting rejection should be withdrawn.

V. Conclusion

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

The Examiner is invited to contact the undersigned with any questions or concerns with the filing of this paper.

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Respectfully submitted,

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